PATENT
Attorney Docket No: 03495-0008-09

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of)
)
Marc ALIZON et al.) Group Art Unit: 1648
)
Serial No.: 08/466,921) Examiner: J. PARKIN
)
Filed: June 6, 1995)
)
For: HIV-1 DNA FRAGMENTS THAT)
HYBRIDIZE TO GENOMIC)
HIV-1 DNA (As Amended))

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY BRIEF

In response to the Examiner's Answer dated September 13, 2000, Appellants submit the following remarks.

REMARKS

1. Issues resolved by the Examiner's Answer

In the Examiner's Answer dated September 13, 2000, the Examiner stated that "The summary of the invention contained in the brief is correct." (Examiner's Answer at 2.) Accordingly, the Examiner does not dispute the following.

Appellants were the first to create cDNA clones of HIV-1. (Brief at 3, ¶ 2.)

Appellants amplified cDNA clones of HIV-1 and cross-hybridized their HIV-1 fragments. (*Id.*)

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Appellants generated HIV-1 restriction fragments. (*Id.* at 4, ¶ 1.)

Appellants performed Southern blotting of isolated HIV-1 restriction fragments. (*Id.* at 4, ¶ 2.)

Appellants hybridized HIV-1 DNA to HIV-1 restriction fragments. (*Id.*)

Appellants used the recited hybridization conditions with HIV-1 DNA. (*Id.* at 5, ¶ 1.) Under these conditions, no non-specific hybridization was seen. (*Id.*)

Appellants are claiming HIV-1 DNA fragments, which hybridize to the genomic DNA of HIV-1 under these conditions. (*Id.*)

Furthermore, the Examiner made additional statements that help to resolve issues on appeal.

The Examiner stated: "[T]he disclosure describes similar hybridization conditions to those claimed by applicants . . . " (Examiner's Answer at 5, lines 4-6.) Thus, the Examiner concedes that Appellants were in possession of the claimed hybridization conditions.

The Examiner further stated: "Appellants assert that they were in possession of what appear to be two-full length proviral molecular clones of LAV (or HIV-1) designated λ-J19 and λ-J81.

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The Examiner does not dispute this assertion." (*Id.* at 8, line 30, through 9, line 1.) Thus, the Examiner concedes that Appellants were in possession of full-length HIV-1 DNA.

The Examiner also stated: "Appellants also assert that they were in possession of specific LAV restriction fragments. The Examiner does not dispute this finding . . . ." (*Id.* at 9, lines 2-4.) Thus, the Examiner concedes that Appellants were in possession of HIV-1 restriction fragments.

Moreover, the Examiner recognizes that "the claims encompass an exceedingly large genus of nucleic acids encompassing small fragments from 10-15 nt to full-length proviral genomes (~10 kb)." (*Id.* at 7, ¶ 3.) Nevertheless, the Examiner did not contest Appellants' argument that Appellants' restriction fragments are representative of the claimed genus of HIV-1 fragments. (Brief at 17-19.) Appellants submit that the Examiner's lack of specific response to their arguments evidences the incontrovertibility of these arguments. Thus, Appellants' restriction fragments should be considered by the Board to be representative of the claimed genus of HIV-1 fragments.

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2. **Rejection under 35 U.S.C. § 112, first paragraph**

In light of the above concessions by the Examiner, there can be no doubt that:

Appellants had possession of clones of the complete HIV-1 genome;

Appellants had possession of HIV-1 restriction fragments;

Appellants hybridized HIV-1 restriction fragments specifically to genomic HIV-1 DNA;

Appellants made amplified copies of HIV-1 restriction fragments; and

Appellants had possession of the recited hybridization conditions.

However, the Examiner appears to conclude that Appellants were not in possession of the claimed invention simply because it was not described in *ipsis verbis*. That is, it is the Examiner's position that the specification does not specifically describe using the claimed hybridization conditions for detecting HIV-1 fragments, but rather, describes these conditions in a hybridization for a different purpose. However, an *ipsis verbis* description of the invention is not required. In re Wertheim, 541 F.2d 257, 265, 191 U.S.P.Q. 90, 98 (C.C.P.A. 1976).

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Rather, the specification **as a whole** must be considered to determine whether the specification describes the claimed invention. In re Wright, 866 F.2d 422, 424, 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989). Appellants' specification, when read **as a whole** and not piecemeal, demonstrates that Appellants contemplated the claimed invention.

Appellants did not contemplate using only a single hybridization condition in their invention. Rather, Appellants recognized, as would the skilled artisan, that many different conditions could be used, including the claimed conditions. What was important was that the DNA was "hybridizable." (*See, e.g.*, Specification at 1, lines 1-23 and Title.)

The Examiner, without any supporting documentation, contends that "the claimed invention recites low stringency conditions which would not be conducive to the identification of HIV-1-specific probes or fragments." (Examiner's Answer at 7, ¶ 3.) However, the Examiner's own statements in the Examiner's Answer show that this contention is in error.

That is, the Examiner recognizes that, under Appellants' claimed conditions, "no hybridization was detected after two days exposure at -70°C using an intensifying screen." (Examiner's Answer at 6-7, quoting the specification.) As

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recognized by the Examiner, this section of the specification assessed hybridization to other known retroviruses. (*See id.*) Consequently, this section of the specification indicated a lack of **non-specific** hybridization of HIV-1 genomic DNA to other DNAs under non-stringent conditions. At the same time, it cannot be disputed that HIV-1 genomic DNA **would** hybridize to HIV-1 fragments under these conditions. This conclusion is reinforced by the hybridization of HIV-1 genomic DNA to HIV-1 fragments under conditions of greater stringency, for example, stringent conditions. (*See, e.g.*, Specification at 10-11, bridging ¶.) In other words, even non-stringent conditions are specific conditions for hybridization to HIV-1 genomic DNA. Therefore, in contrast to the Examiner's contention, Appellants hybridization conditions are, in fact, "conducive to the identification of HIV-1-specific probes or fragments."

The specification teaches that Appellants' invention encompasses HIV-1 DNA fragments that hybridize to HIV-1 genomic DNA. The skilled artisan would immediately recognize that the claimed hybridization conditions, as taught by the specification, are conditions under which HIV-1 DNA fragments would hybridize to HIV-1 genomic DNA. Therefore, the skilled artisan would recognize that Appellants had possession of the

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claimed invention at the time the application was filed. Reversal of the rejection of claims under 35 U.S.C. § 112, first paragraph, on the ground of lack of an adequate written description is respectfully requested.

3. Rejection under 35 U.S.C. § 112, second paragraph

In the Examiner's Answer dated September 13, 2000, with respect to the word "amplified" in claims 68 and 69, the Examiner stated that "the disclosure fails to define this term and that Appellants have failed to provide any publications that provide a clear and concise explanation of the term as it is applied in the art." (Examiner's Answer at 6.) The Examiner's position is in error.

As Appellants pointed out in their July 16, 1999, Amendment and Response to Paper No. 26:

> The specification teaches the generation of a single-stranded DNA copy of HIV-1 RNA, and subsequent generation of a double-stranded DNA copy. (*Id.* at 7). The specification teaches the insertion of this DNA into a vector and the small-scale amplification of clones containing HIV-1 fragments. (*Id.* at 7-8). The amplified inserts were analyzed by hybridization. (*Id.* at 8). It was found that the clones were copies of the 3' end of a polyA-RNA. (*Id.* at 8, paragraph 3). Therefore, the skilled artisan would recognize that the invention encompasses amplified copies of HIV-1 DNA fragments, as recited in claim 68.

(July 16, 1999, Amendment and Response to Paper No. 26 at 5.)

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Furthermore, the specification specifically recites the word "amplification":

> A major family was obtained by small-scale **amplification** of these clones and cross-hybridization of their inserts.

(Specification at 7.)

In addition, the specification specifically recites the word "amplifiable":

> The invention also relates more specifically to cloned probes which can be made starting from any DNA fragment according to the invention, thus to recombinant DNAs containing such fragments, particularly any plasmid **amplifiable** in procaryotic or eukaryotic cells and carrying said fragments.

(Specification at 7.)

Having read the disclosure, the skilled artisan would have no doubt that Appellants were using the word "amplified" simply to refer to copies of the claimed DNA fragment that have been further copied regardless of how the amplification was performed. Appellants' claimed invention is not limited to any particular amplification process.

Appellants further point out that the fact that "amplified" encompasses "PCR amplified" HIV-1 fragments **is not relevant** to a rejection under 35 U.S.C. § 112, second paragraph because the

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Polymerase Chain Reaction (PCR) was not publicly available until **after** Appellants' filing date.[1]

The Federal Circuit has stated that definiteness must be assessed as of the application's filing date, and that post-filing date developments are irrelevant to this assessment. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 1556, 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983)("[S]ubsequently developed and therefore irrelevant formulae cannot be used to render non-enabling or indefinite that which was enabling and definite at the time the application was filed."). Therefore, PCR, which was discovered **after** Appellants' filing date, is irrelevant to the definiteness of Appellants' claims.

Furthermore, the Examiner has not indicated how a later discovery can possibly be relevant to the clarity of Appellants' claimed invention. Importantly, the Examiner has provided no explanation of how a later discovery can introduce indefiniteness into Appellants' claims, which were definite as of Appellants' filing date.

The rejection of claims 68 and 69 under 35 U.S.C. § 112, second paragraph, should be reversed.

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[1] Appellants assume that the Examiner's reference to "PCR" is to the process first published in the December 20, 1985, issue of *Science*. Saiki et al., *Science* 230:1350-4 (1985). This publication is **after** Appellants' filing date.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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